ABSTRACT: Objectives: Report the efficacy of open-label amphetamine extended-release oral suspension (AMPH EROS) for the treatment of children with ADHD.
AMPH EROS has a 1-hr onset of effect and a duration of action of 13 hours and was approved by FDA for treatment of ADHD in children aged 6–17 years based on a double-blind, placebo-controlled efficacy and safety study in children aged 6–12 years with ADHD. A significant treatment difference in change from pre-dose SKAMP-combined score was observed at the primary endpoint of 4 hours post-dose ($p < 0.0001$) and each post-dose time point assessed (1, 2, 4, 6, 8, 10, 12, 13 hours).
Data reported here are from the 5-week, open-label dose optimization period. These efficacy data support the primary endpoint result.

METHODS: Males and females aged 6 to 12 years with ADHD enrolled and began open-label treatment with 2.5 mg or 5 mg/day of AMPH EROS titrated in 2.5–10 mg/day increments until optimal dose (maximum 20 mg/day). Doses could be decreased for tolerability. Subjects took morning AMPH EROS for 5 weeks. Other efficacy outcomes during the open-label dose optimization phase: ADHD-RS (ADHD-Rating Scale), CGI-S (Clinical Global Impression of Severity), CGI-I (CGI-of Improvement) and CPRS (Conners' Parent Rating Scale). All subjects were assessed for safety.

RESULTS: For the ITT population ($n = 99$): treatment with AMPH EROS was associated with a mean change in ADHD-RS-IV (baseline to end of the open-label dose optimization; week 6) of 28.2 (±9.03) (Baseline score = 41.3±7.95). 90.9% of subjects had a change from baseline to open-label week 6 of ≥50% in the ADHD-RS-IV total score and were defined as responders. The CGI-S scores decreased continuously from baseline, with a high 4.8 at baseline to a low of 2.0 at open-label week 6. The percentage of subjects classified as moderately ill or greater correspondingly decreased from 97% at Baseline to 1% at open-label week 6. The decrease in the CGI-I over the study was similar to the change in CGI-S scores. CPRS for most categories decreased continuously from Baseline to open-label week 6. Mean change from baseline to open-label week 6 on the CPRS inattention T-score subscale was –25.3 (±14.38) and –24.4 (±13.87). Adverse events (>5%) reported during dose optimization were decreased appetite, insomnia, affect lability, upper abdominal pain, mood swings and headache.

CONCLUSION: AMPH EROS was effective in reducing symptoms of ADHD in this open-label dose optimization. The AE profile of AMPH EROS was consistent with those of other amphetamine products.
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The Efficacy and Safety of Amphetamine Extended-Release Oral Suspension (AMPH EROS) in Children with Attention-Deficit/Hyperactivity Disorder

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ABSTRACT: OBJECTIVES: To determine the efficacy and safety of amphetamine extended-release oral suspension (AMPH EROS) in the treatment of attention-deficit/hyperactivity disorder (ADHD) compared with placebo in a dose-optimized, randomized, double-blind study.

METHODS: The efficacy of AMPH EROS was evaluated in a laboratory classroom study conducted in 108 pediatric patients (aged 6–12 years) with ADHD. The study began with an open-label dose optimization (5 weeks) with an initial AMPH EROS dose of 2.5 or 5 mg once daily in the morning. The dose could be titrated every 4–7 days in increments of 2.5–10 mg until an optimal dose or the maximum dose of 20 mg/day was reached. Subjects were required to tolerate a minimal dose of 10 mg/day. Subjects then entered a 1-week randomized, double-blind treatment phase with the individually optimized dose or placebo. At the end of the week, raters evaluated the attention and behavior of the subjects in a laboratory classroom using the Swanson, Kotkin, Agler, M-Flynn, and Pelham (SKAMP-C) rating scale. SKAMP-C is a 13-item teacher-rated scale that assesses manifestations of ADHD in a classroom setting.
The primary efficacy endpoint was change from pre-dose in the SKAMP-C score at 4 hours post dose. The key secondary endpoint efficacy parameters were onset and duration of clinical effect. The change scores from pre-dose SKAMP-C scores at post dose time points (1, 2, 6, 8, 10, 12 and 13 hours) were used to evaluate the key secondary efficacy endpoints.

RESULTS: More boys (68.7%) than girls participated in the study. The study population was 55.6% white, most patients had inattentive or combined type ADHD presentations. The primary efficacy endpoint, the change from pre-dose SKAMP-C score at 4 hours post dose was statistically significantly improved ($p < 0.0001$) compared with placebo. Each of the secondary efficacy endpoints were also significantly improved ($p < 0.0001$ at each time point) compared with placebo. Adverse events reported (frequency >5%) reported during the dose optimization

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phase were decreased appetite, insomnia, affect lability, upper abdominal pain, mood swings, and headache.

CONCLUSIONS: AMPH EROS was effective in reducing symptoms or ADHD from 1 to 13 hours after dosing. Adverse events reported were consistent with those of other amphetamine products.

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A Novel, Modified-Release Drug Delivery Technology Containing Amphetamine-Ion Exchange Complexes

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ABSTRACT: The proprietary immediate and extended drug delivery technology LiquiXR™ utilizes an ion-exchange resin that complexes with amphetamine or any other active moiety that can be protonated and is water-soluble. The active drug product forms a complex with ion-exchange polymers contained in the resin, which is then formed into micron-sized particles. Some of these particles are coated with an aqueous, pH-independent polymer designed to provide immediate or sustained release of active drug product. The polymer coating applied to the ion-exchange resin particles is of varying thickness, allowing for programmed, extended release of active drug product. Solid, coating-free particles provide for immediate release of active drug product.

The micron-sized particles are formulated into an appropriate dosage form (solid or chewable tablet, liquid suspension, orally disintegrating tablet, film, or capsules). Active drug product is subsequently released from the dosage form in millions of particles, with the release driven by a combination of ion exchange and diffusion. After drug release, the ion-exchange resin is excreted in the feces.

The release characteristics of LiquiXR™ are programmable and allow for a customized, sustained release of active drug product for up to 24 hours post-dose. Mechanistically, drug particles enter the gastrointestinal tract. As positively-charged ions from gastrointestinal (GI) fluids diffuse across the coating, ionically-charged drug product diffuses through the coating and into the GI fluids for absorption. As the coating is of variable thickness, some drug product takes longer to diffuse and absorb, providing for the programmable delayed drug release characteristic.

The LiquiXR™ drug delivery technology is utilized in Dyanavel® XR (amphetamine extended-release oral suspension; AMPH EROS), which is indicated for the treatment of attention-deficit hyperactivity disorder. It comprises 2.5 mg/mL amphetamine base complexed with LiquiXR technology to provide an immediate release component followed by an extended-release profile. The efficacy of AMPH EROS was established in children ages 6 to 12 years in a Phase 3, placebo-controlled laboratory classroom study. In that study, attention-deficit/hyperactivity disorder (ADHD) symptoms in children on an individually optimized dose of amphetamine (range 10–20 mg/day) were statistically significantly improved compared with symptoms in children treated with placebo. For children treated with AMPH EROS, onset of effect was demonstrated at 1 hour after dosing, and efficacy was observed through 13 hours post-dose. The effect size was comparable to effect sizes demonstrated for other psychostimulants tested in studies using a similar design. The efficacy data reported for AMPH EROS provides an excellent example of the potential utility and clinical application for other active drug products requiring an immediate release and extended release profile.

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Effects of Smartphone Coaching Intervention on Dietary Intake for Bariatric Surgery Candidates: A Pilot Randomized Controlled Trial

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ABSTRACT: Introduction: Bariatric surgery outcomes are variable, often with suboptimal weight loss and/or weight relapse. Smartphone coaching applications offer a potential window of affecting behavioral change to improve outcomes in a widespread and cost-effective way, but clinical efficacy is unknown. In phase I of this pilot study, we investigated effects of pre-surgical treatment with a mobile coaching platform Noom Coach for Bariatric Health.

METHODS: Forty adult candidates (82.5% female) for bariatric surgery were recruited for pilot randomized

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